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Effect of troxerutin on synaptic plasticity of hippocampal dentate gyrus neurons in a β-amyloid model of Alzheimer's disease: An electrophysiological study

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ABSTRACT

Alzheimer's disease (AD) is a neurodegenerative disorder with a progressive cognitive decline and memory loss. Multiple pathogenetic factors including aggregated β-amyloid (Aβ), neurofibrillary tangles (NFTs), cholinergic dysfunction and oxidative stress are involved in AD. Aβ, a major constituent of the senile plaques, is a potent neurotoxic peptide and has a pivotal role in cognitive deficit and reduced synaptic plasticity in AD. In the present study we examined the protective effect of troxerutin, as a multipotent bioflavonoid, on Aβ (1–42)-induced impairment of evoked field potential in hippocampal DG neurons. Male Wistar rats were divided into four groups including Aβ (42–1), Aβ (1–42), Aβ (1–42) plus troxerutin and Aβ (42–1) plus troxerutin groups. Aβ was injected intracerebroventricularly (i.c.v.) into right lateral ventricle and after two weeks the evoked field potential recorded from perforant path-DG synapses to assess paired pulse paradigm and long term potentiation (LTP). Administration of Aβ (1–42) drastically attenuated the LTP of DG neurons, while there was no significant difference in evoked field potentials between Aβ (1–42) plus troxerutin group with respect to Aβ (42–1) group. This study revealed that troxerutin improves the synaptic failure induced by Aβ peptide and can be introduced as a promising multi-potent pharmacological agent in prevention or treatment of AD in the future.

1. Introduction

Accumulation of amyloid-beta peptide (Aβ) in the brain of patient with Alzheimer's disease (AD) leads to neuronal dysfunction and cognitive deficits (Selkoe, 2001). Memory deficit in AD begins with changes in hippocampal synaptic functions and then gradually promotes toward subsequent neurodegeneration and neuronal loss in these patients (Selkoe, 2002). A main form of synaptic plasticity is long-term potentiation (LTP) which is an activity-dependent increase in synaptic efficiency. Hippocampal LTP is well recognized as a cellular basis of learning and memory and provides an attractive means of detecting any changes in synaptic function (Namgung et al., 1995). Surveys conducted by previous researchers have shown that LTP undergoes changes by Aβ in the hippocampus resulting in cognitive dysfunction and impairment of learning and memory (Babri et al., 2012a; Selkoe, 2008).

Multiple factors such as Aβ aggregation, the formation of neurofibrillary tangles (NFTs), cholinergic dysfunction, inflammatory agents, oxidative stress and glutamate-mediated excitotoxicity are involved in the pathogenesis of AD, the factors can act somehow to alter the synaptic efficacy (Querfurth and LaFerla, 2010). Previous strategies to combat AD have led to discovering drugs aimed at single targets, e.g. β-secretase, N-methyl-D-aspartate (NMDA) receptors, acetylcholinesterase (AChE) enzyme and reactive oxygen species and a little attention has been paid to introduce a multipotent agent aiming at different targets (Francis et al., 2010; Li et al., 2010). The recent studies have emerged that using natural products especially the flavonoids which possess

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